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Request for grant of a patent

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1. Your reference — P64961/000

2. Patent application number *(The Patent Office will fill this part in)* — 0329725.6

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

   Bioquell UK Limited
   Walworth Road
   Andover, Hampshire
   SP10 5AA

   Patents ADP number *(if you know it)* — 08070930001

   If the applicant is a corporate body, give the country/state of its incorporation — UNITED KINGDOM

4. Title of the invention — APPARATUS AND METHOD FOR BIO-DECONTAMINATION OF AN ENCLOSURE

5. Name of your agent *(if you have one)* — BOULT WADE TENNANT

   "Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

   VERULAM GARDENS
   70 GRAY'S INN ROAD
   LONDON
   WC1X 8BT

   Patents ADP number *(if you know it)* — 42001 ✓

6. Priority: Complete this section if you are declaring priority from one or more earlier patent applications, filed in the last 12 months.

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. Divisionals, etc: Complete this section only if this application is a divisional application or resulted from an entitlement dispute (see note f)

Number of earlier UK application	Date of filing *(day / month / year)*

8. Is a Patents Form 7/77 (Statement of inventorship and of right to grant of a patent) required in support of this request? — YES

   Answer YES if:
   a) any applicant named in part 3 is not an inventor, or
   b) there is an inventor who is not named as an applicant, or
   c) any named applicant is a corporate body.
   Otherwise answer NO (See note d)

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	14
Claim *(s)*	3
Abstract	0
Drawing *(s)*	5 + 5 fm

10. If you are also filing any of the following, state how many against each item.

Priority documents	0
Translations of priority documents	0
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	0
Request for preliminary examination and search *(Patents Form 9/77)*	0
Request for substantive examination *(Patents Form 10/77)*	0
Any other documents *(please specify)*	0

11. I/We request the grant of a patent on the basis of this application.

Signature — Date 22 December 2003

12. Name and daytime telephone number of person to contact in the United Kingdom 020-7430-7500

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Apparatus and Method for Bio-decontamination of an Enclosure

This invention relates to apparatus and methods for the bio-decontamination of enclosures and in particular small enclosures. Such enclosures are typically up to about $2m^3$ in volume, and include but are not limited to Class II Microbiological Safety Cabinets (MSC). Our International Patent Application GB03/001386 discloses methods of bio-decontaminating larger enclosures such as rooms or chambers by placing an apparatus to generate the fumigant gas inside the chamber. The technique described works well for rooms and large chambers of a simple nature but is not specifically intended to deal with the problems associated with Class II microbiological safety cabinets and similar enclosures.

The standard technique for bio-decontaminating a Class II MSC is to boil formalin to generate formaldehyde vapour. For this method to be effective substantial amounts of formalin have to be evaporated, the European Standard EN BS 12469 requires 60ml of formalin plus 60ml of water to be evaporated for each cubic metre of enclosure volume. Other authorities use smaller amounts of liquid but all of the methods used generate considerable amounts of condensation within the MSC and also form deposits of paraformaldehyde.

Formalin gassing of an MSC has a number of disadvantages; firstly it leaves a residue of formalin and paraformaldehyde that can only be removed by long periods of aeration; secondly the bio-decontamination process is slow, the normal exposure time being eight hours; thirdly it is difficult to ensure that the gas has reached all parts of the MSC

especially in the filter plenum, fourthly the vapour is toxic with an Occupational Exposure Limit of 1 ppm, and lastly special precautions have to be taken to avoid leakage of the gas from the MSC, and in some installations the laboratories have to be evacuated during the fumigation process. An alternative to formalin fumigation that overcomes these problems would be of considerable value to laboratory personnel, and one choice of fumigant is hydrogen peroxide vapour providing that it can be deployed in a way which is safe for the user, since it is residue free, is effective and is fast acting.

It may be expected that some of the same difficulties that are encountered with formalin will also be encountered when using hydrogen peroxide as a fumigant. Most, if not all, MSCs leak to some extent. Introducing gas inside a chamber is accompanied by a rise in temperature which causes an increase in internal pressure. This rise in pressure, unless it is controlled, leads to leakage of the fumigant gas to the outside giving rise to a potential hazard to laboratory staff. Hydrogen peroxide and formaldehyde have similar diffusion constants and so it may be expected that the rate at which these two gases would diffuse around the enclosure would be similar. In an MSC it may be expected that bio-decontamination of the plenum chamber using hydrogen peroxide vapour may take some considerable time unless techniques are used to cause the gas to travel into the plenum.

The main advantages of using hydrogen peroxide as the fumigant gas are the facts that it does not leave a residue and that once an adequate gas concentration has been reached

the process is very fast. Many, if not most, Class II MSCs that are in use recirculate their exhaust air back to the laboratory, and hence a method is required to remove the hydrogen peroxide vapour at the end of the bio-decontamination cycle.

The present invention is a technique to overcome these problems and provide a safe and reliable way to bio-decontaminate small enclosures including MSCs.

This invention provides an enclosure for carrying out an operation under sterile conditions having a first apparatus disposed within the enclosure for generating and delivering a sterilant vapour from a supply held within the enclosure to condense on surfaces throughout the enclosure to sterilise the surfaces, and means to draw gas from the enclosure at a location remote from the apparatus for delivering the sterilant to the enclosure to ensure that the sterilant vapour reaches the most remote part of the enclosure from the location where the sterilant is delivered to the enclosure and to maintain the enclosure at a predetermined pressure below atmospheric so that any leak paths result in leakage from the atmosphere into the enclosure and do not release sterilant vapour to atmosphere around the enclosure.

In accordance with one embodiment of the invention the means for drawing gas from the enclosure comprise a fan located in a conduit connected to an outlet from the enclosure, the conduit having means to render sterilant reaching the conduit ineffective to avoid release of sterilant to atmosphere.

Preferably the means to render the sterilant ineffective are located upstream of the fan in relation to the enclosure.

More specifically the means to render the sterilant ineffective may comprise a catalytic converter for breaking the sterilant down into harmless biproducts which can be exhausted to atmosphere.

It is also preferred that the conduit has selectively operable valve controlled outlets of larger and smaller capacities, the smaller capacity outlet being open during said period when the enclosure is to be maintained at a predetermined reduced pressure and the larger valve controlled outlet being opened during discharge of the sterilant atmosphere from the enclosure.

In any of the above arrangements, the enclosure may have a main chamber containing said apparatus for producing sterilant vapour and within which the operation to be carried out in the chamber is performed and a plenum chamber separated from the main chamber by a filter, the plenum chamber having a pump for delivering air into the plenum chamber through the filter to the main chamber to create a filter flow of air through the chamber and the means for drawing gas from the chamber remote from the first apparatus is connected to the plenum chamber.

In the latter arrangement a filter may be provided in the outlet from the plenum chamber to the means for drawing gas from the plenum chamber.

Also in any of the above arrangements the enclosure may contain a second apparatus for rendering sterilant in the atmosphere in the chamber ineffective after the sterilisation of the chamber.

In the latter construction the means for rendering sterilant ineffective may comprise a housing containing a catalytic converter for converting the sterilant into harmless biproducts for disposal and means for circulating the atmosphere of the chamber through the housing to reduce the sterilant concentration in the atmosphere when the sterilisation operation has been performed.

The following is a description of some specific embodiments of the invention, reference being made to the accompanying drawings in which:

Figure 1 is a schematic view of a Class II Microbiological Safety Cabinet incorporating an internal sterilant vapour producing device, an internal vapour decomposition device and an external pressure regulation and aeration system;

Figure 2 is a more detailed schematic view of the sterilant vapour producing device of Figure 1;

Figure 3 is a more detailed schematic view of the vapour decomposition device of Figure 1;

Figure 4 is a more detailed schematic view of the external pressure regulation/aeration system of Figure 1; and

Figure 5 is a schematic view of the complete apparatus of Figure 1 in operational mode.

The apparatus is made up from three parts. The first part is a gas generator as disclosed in our International Patent Application GB03/001386. The gas generator is placed inside a main chamber of a cabinet. In the following description this will be an MSC, but it could be any small enclosure. Placing the generator inside the enclosure has the considerable advantage that holes do not have to be made in the MSC to connect supply and exhaust gas hoses. The generator consists of a hot plate, maintained at a temperature in excess of the boiling point of the aqueous hydrogen peroxide solution, onto which the solution of hydrogen peroxide is fed. A stream of air and gas mixture is blown across the heated plate to drive the vapours into the main chamber of the MSC. Also housed in the gas generator is the bottle containing the hydrogen peroxide solution, the volume of solution in the bottle is adjusted so that it is sufficient when evaporated to bio-decontaminate the MSC. This volume will vary according to the size and type of MSC. Attached to the gas generator is an external fan, set to drive the air/gas mixture from the main chamber through the internal pathways of the MSC. This ensures that the hydrogen peroxide and water vapour reach the internal plenum of the MSC.

The second unit is also placed inside the main chamber of the MSC and may be used to remove the hydrogen peroxide vapour at the end of the gassing cycle. This second unit works by passing the air gas mixture through a catalyst bed thus decomposing the hydrogen peroxide to water and oxygen.

The third unit is placed outside the MSC and has the dual function of maintaining a negative pressure during the gassing phase of the bio-decontamination cycle and afterwards may be used to remove the air/gas mixture rendering the exhaust gas harmless, by decomposing it to water and oxygen.

All three of these parts of the system are connected to a central control unit which is placed outside the MSC, giving the operator complete control of the process. A single electrical cable connects the units inside the MSC to the control system.

Experimental work was carried out to see if it is possible to bio-decontaminate an MSC while maintaining it under negative pressure, thus minimising outward leaks thereby ensuring a safe environment around the MSC, and also to reduce the time taken for bio-decontamination to a minimum using an automated cycle that would run without any input from the operator once the cycle had been started.

The specification for fumigation with formaldehyde requires that the main down flow fan inside the MSC has to be run during the gassing cycle. This means that either the MSC has an automated formaldehyde gassing cycle or the operator is required to attend during the cycle to switch the fan on and off. The reason for operating the fan is to ensure that the formaldehyde gas reaches the main plenum chamber. Ideally the cycle should not require an operator to attend until the cycle is completed.

A gassing cycle was arranged in four phases, the first to allow the equipment to stabilise, the second to evaporate the required amount of aqueous hydrogen peroxide solution thus raising the gas concentration and causing the formation of condensation on the surfaces, the third to maintain the chamber in this condition for a sufficient period of time to ensure bio-decontamination to the required standard, and finally to remove the air/gas mixture rendering the chamber safe.

A series of experiments were conducted to establish the best gassing cycle and equipment configuration to achieve a reliable bio-decontamination in the shortest possible time. The tests were conducted using a Class II MSC with the cabinet configured to recirculate the air back to the laboratory and also to duct the exhaust air to the outside. When in the recirculatory configuration it is essential that the exhaust air returned to the laboratory contains less than 1ppm of hydrogen peroxide. If the exhaust air is to be exhausted to the outside it is possible to use the MSC extract fan to remove the hydrogen peroxide vapour, and thus reduce the aeration time.

There are two reasons for wanting to bio-decontaminate an MSC, they are to ensure that the working chamber is free of biological contamination and hence will not contaminate any experimental work undertaken inside the Cabinet, and the second is to ensure that the whole MSC is free of biological contamination so that the necessary maintenance operations, such as a filter change, may be undertaken without risk to the service and laboratory staff.

The tests reported here show the difference in the amount of liquid required to bio-decontaminate the chamber as compared with the whole MSC. This difference is a measure of the difficulty of achieving total bio-decontamination. For a test to be considered to give a satisfactory result it had to be conducted three times and give consistent results. The table below shows a summary of these tests.

Configuration	Ducted	Recirculatory	Ducted	Recirculatory
Pressure Point	Chamber	Top	Top	Top
Liquid Volume ml	10	15	65	65
Bio-decontamination	Chamber	Chamber	All	All
Total Cycle Time min.	36	85	?	160

Pressure control of the MSC is critical not only to contain the active gas but may also be used to distribute the active gas throughout the whole MSC. In the first test reported above the pressure control point was in the wall of the main chamber of the MSC, but by moving this control point to the top of the MSC as in tests 3 and 4 the active gas is caused to circulate to all areas of the MSC. Negative pressure control is achieved by extracting a small amount of the active gas, thus causing the gas to move towards the pressure control point, and hence by placing the control point at the greatest distance from the injection point the gas is distributed throughout the whole MSC. A similar argument would apply to any complex chamber.

Further confirmation of the effects caused by the extraction point may be seen from the table below, which shows the gas concentration in the top fan plenum Chamber. The readings were taken at intervals of 5 minutes, and a note was taken of the highest value.

Top Pressure Control Ppm	Chamber Pressure Control Ppm	Time Minutes
0	0	0
34	7	10
79	12	20
85	7	30
120	9	40
159	13	50
183	18	55
763	124	60
902	448	Maximum

It can be seen from the above table that the gas concentration in the remote part of the MSC is much higher with the pressure control in the top of the cabinet than when it is in the chamber. This improved gas distribution leads to a reliable and faster bio-decontamination throughout the whole of the MSC. As stated above a similar technique would work for other types of complex chambers.

The apparatus of the invention is composed of four parts to minimise the weight of a single component so that it may easily be carried and set up by one person. These four parts will now be described in turn in conjunction with the

method of operation with reference to Fig 2, 3, 4 and 5. The configuration shown in these diagrams is intended to be illustrative and not exclusive. There are a number of alternative configurations of enclosure which would allow changes to the set up.

Referring firstly to Fig 5 which depicts a typical Class II MSC 23 with an internal Fan 21 a down flow filter 24 and an exhaust filter 22. Class II MSC are constructed in accordance with EN BS 12469, and generate a vertical down flow of air that has passed through a sterilising filter, a proportion of the air is exhausted either to the outside or recirculated to the room through the filter 22. The Cabinet is so constructed so that the outer surface is under negative pressure thus preventing leakage to the room. Fig 5 depicts a typical set up for a recirculating Cabinet.

The hydrogen peroxide generator 17 and a small aeration unit 18 are placed inside the main chamber of the MSC. They are connected to a Control Module 20 that is outside the MSC by an electrical cable. An external pressure control and aeration unit 19 are placed outside the MSC and also connected to the Control Unit 20. A further duct connection is made to the pressure control and aeration unit so that air may be exhausted from the spigot on the top of the MSC.

The method of operation of each of these components will now be described with reference to the diagrams.

The evaporation unit is shown in Fig 2, and consists of a liquid reservoir 2 housed in a case 6 with a perforated top and bottom to allow air to freely pass through the case. The case is mounted on feet 7 to minimise contact with the

surface and allowing free passage of air all round the external surfaces. A fan 4 draws air in at the bottom of the case and causes a flow of air over the internal components and then to exhaust from the top of the Case 6. A heater 3 is placed in the air stream to raise the temperature of the air. A heater plate 1 is positioned above the air heater 3 on to which hydrogen peroxide solution is delivered by the pump 2A and pipe 2B. The hydrogen peroxide solution is evaporated on the heated plate 1 which is maintained at a temperature above the boiling point of the solution. The heated air stream carries the water and hydrogen peroxide vapours out of the case 6, and part of this hot air/vapour stream is deflected by the external fan 5. In order to achieve rapid and reliable bio-decontamination it is essential that the vapours are distributed to all areas of the chamber while they are still hot. The purpose of the Fan 5 is to ensure the distribution of the vapours immediately that they emerge from the generator. In Class II MSC the air from the working chamber is drawn under the work surface and then up to the fan, the fan 5 may be used to direct the hot vapours into this space. We will return to a more detailed explanation of the gas distribution problems at the end of the description of the apparatus.

The internal aeration unit shown in Fig 3 is used to decompose the hydrogen peroxide vapour to water and oxygen at the end of the bio-decontamination cycle. The unit is contained in a case 10 with a perforated base and top to allow the free passage of air through the unit. It is mounted on feet 11 again to permit the free passage of air all round the unit. Inside the case is a fan 9 which draws the air/gas mixture in at the bottom and forces it through

the catalytic bed 8 that decomposes the hydrogen peroxide vapour, thus reducing the concentration of the vapour inside the Class II MSC by dilution.

The external pressure control and aeration unit is shown in Fig 4. This unit is connected to the exhaust duct at the top of the Class II MSC, and the fan 13 draws air/vapour mixture from the Class II MSC throughout the whole of the bio-decontamination cycle. The air is drawn through a catalytic bed 12 to render the air stream free of harmful hydrogen peroxide vapour. During the gassing phase of the cycle a small amount of air leaves the pressure control aeration unit via the restriction valve 14. This valve is used to control the extract air and hence the internal pressure in the Class II MSC at the same time as causing the hydrogen peroxide vapour to be pulled to the most remote part of the chamber, thus ensuring bio-decontamination in this area. Once bio-decontamination has been achieved the valve 15 is opened and the air flow considerably increased. This increased air flow removes the air/hydrogen peroxide mixture from the inside of the Class II MSC thus reducing the aeration time. During the gassing phase of the cycle the extract air extract will generally be less than $10m^3$ per hour and during aeration this will rise to about $200m^3$ per hour. In order to increase the air flow during the aeration phase it is necessary to allow air into the Class II MSC, this may be achieved by opening the front window of the cabinet by a small amount. In other cabinets a special opening is provided that may be used to allow the inward airflow that is sealed during gassing.

There are a number of alternative configurations of the apparatus, firstly it is not necessary to have the internal aeration unit, although it is helpful in reducing the gas concentration at the start of aeration and avoids the need to open the cabinet to allow an extract system to be operated.

For cabinets that are connected to an exhaust duct the external aeration unit may not be required as the hydrogen peroxide vapour may be vented to the outside using the cabinet fans that have a greater capacity and hence provide a shorter aeration period. It is however still necessary to have a pressure control unit to ensure that the cabinet is maintained at negative pressure and that the gas is properly distributed.

Distribution of the active gas is critical to bio-deactivation process, and because the rate of diffusion is slow it is necessary to use mechanical means, such as fans or extraction, to ensure that the gas reaches all parts of the chamber. In EN BS 12469 for MSC it is suggested that during formaldehyde fumigation that the cabinet internal fan is operated for a short period to move the fumigant to the remote areas of the cabinet. This has the disadvantage of generating high pressure zones inside the cabinet with the consequent risk of leakage.

The fan 5 attached to the evaporator combined with the pressure control extraction system overcomes this problem by direction the hot gas directly into the internal passageways of the chamber. The pressure control system then draws the active gas to the remote parts of the chamber.

CLAIMS

1. An enclosure for carrying out an operation under sterile conditions having a first apparatus disposed within the enclosure for generating and delivering a sterilant vapour from a supply held within the enclosure to condense on surfaces throughout the enclosure to sterilise the surfaces, and means to draw gas from the enclosure at a location remote from the apparatus for delivering the sterilant to the enclosure to ensure that the sterilant vapour reaches the most remote part of the enclosure from the location where the sterilant is delivered to the enclosure and to maintain the enclosure at a predetermined pressure below atmospheric so that any leak paths result in leakage from the atmosphere into the enclosure and do not release sterilant vapour to atmosphere around the enclosure.

2. An enclosure as claimed in claim 1 wherein the means for drawing gas from the enclosure comprise a fan located in a conduit connected to an outlet from the enclosure, the conduit having means to render sterilant reaching the conduit ineffective to avoid release of sterilant to atmosphere.

3. An enclosure as claimed in claim 2, wherein the means to render the sterilant ineffective are located upstream of the fan in relation to the enclosure.

4. An apparatus as claimed in claim 3, wherein the means to render the sterilant ineffective comprise a catalytic converter for breaking the sterilant down into harmless biproducts which can be exhausted to atmosphere.

5. An enclosure as claimed in claim 3 or claim 4, wherein the conduit has selectively operable valve controlled outlets of larger and smaller capacities, the smaller capacity outlet being open during said period when the enclosure is to be maintained at a predetermined reduced pressure and the larger valve controlled outlet being opened during discharge of the sterilant atmosphere from the enclosure.

6. An enclosure as claimed in any of the preceding claims wherein the enclosure has a main chamber containing said apparatus for producing sterilant vapour and within which the operation to be carried out in the chamber is performed and a plenum chamber separated from the main chamber by a filter, the plenum chamber having a pump for delivering air into the plenum chamber through the filter to the main chamber to create a filter flow of air through the chamber and the means for drawing gas from the chamber remote from the first apparatus is connected to the plenum chamber.

7. An enclosure as claimed in claim 6, wherein a filter is provided in the outlet from the plenum chamber to the means for drawing gas from the plenum chamber.

8. An enclosure as claimed in any of the preceding claims, wherein the enclosure contains a second apparatus for rendering sterilant in the atmosphere in the chamber ineffective after the sterilisation of the chamber.

9. An enclosure as claimed in claim 8, wherein the means for rendering sterilant ineffective comprises a housing

containing a catalytic converter for converting the sterilant into harmless biproducts for disposal and means for circulating the atmosphere of the chamber through the housing to reduce the sterilant concentration in the atmosphere when the sterilisation operation has been performed.

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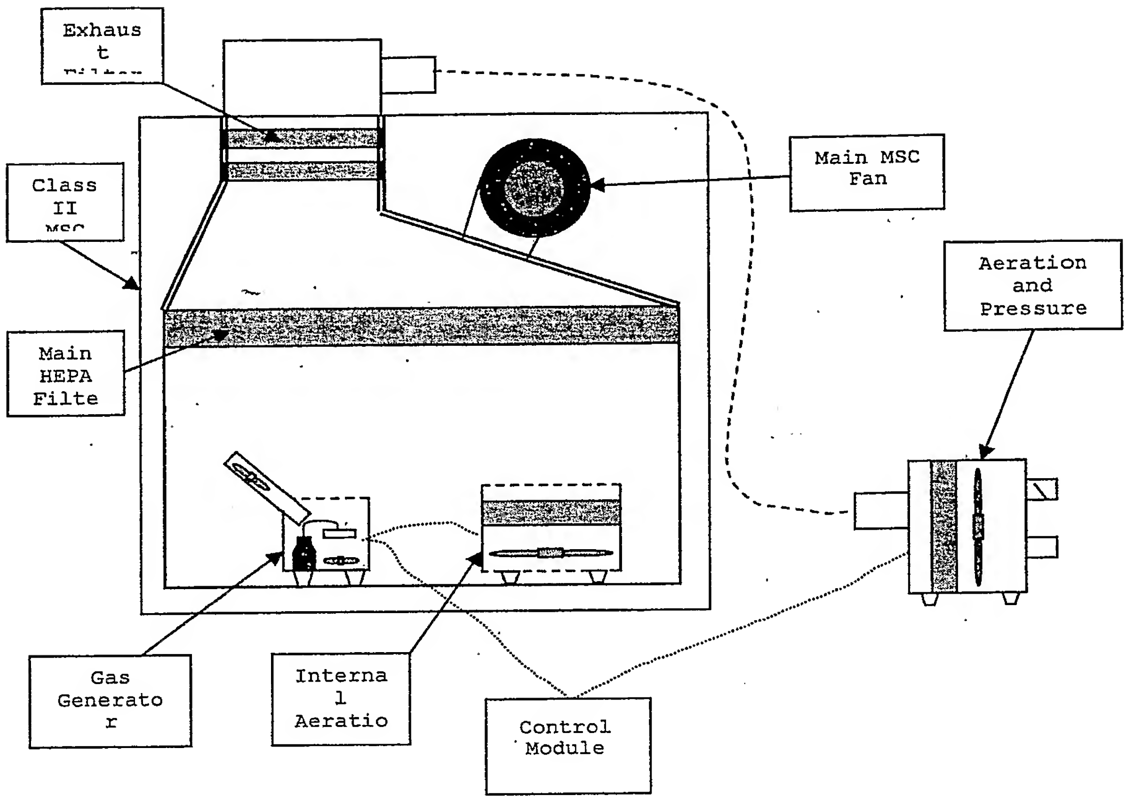
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Fig 1

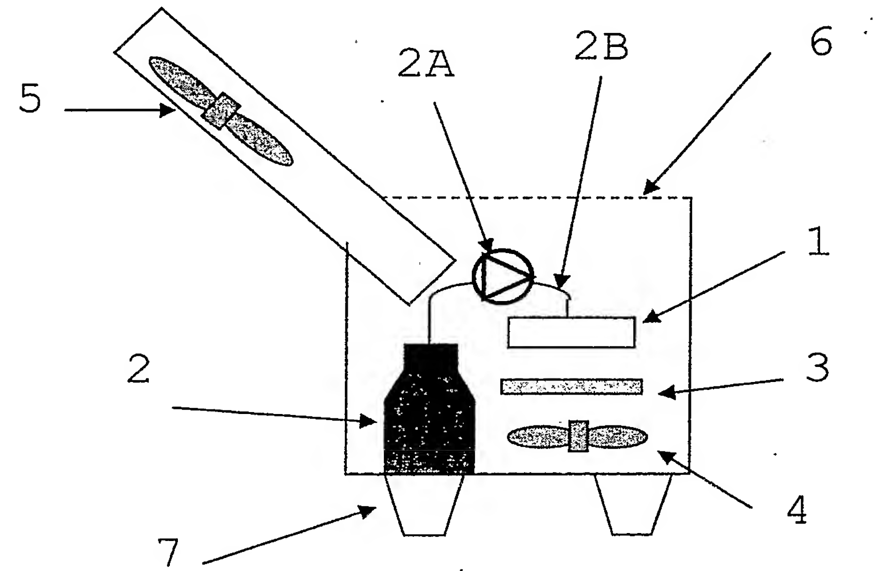

Fig 2

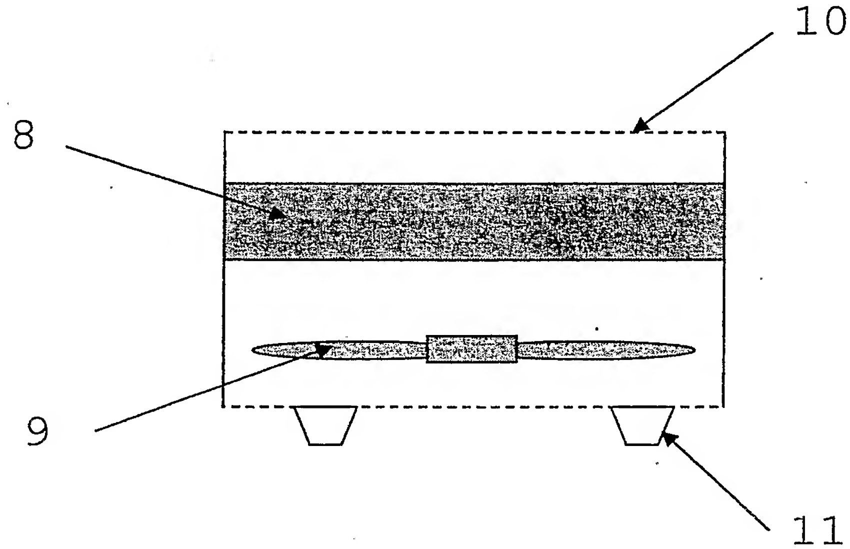

Fig 3

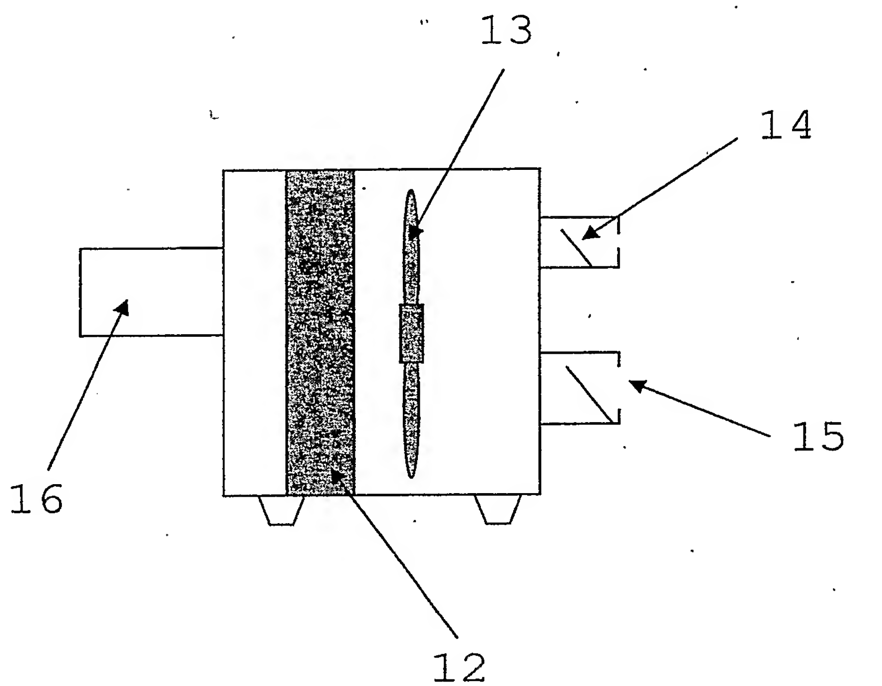

Fig 4

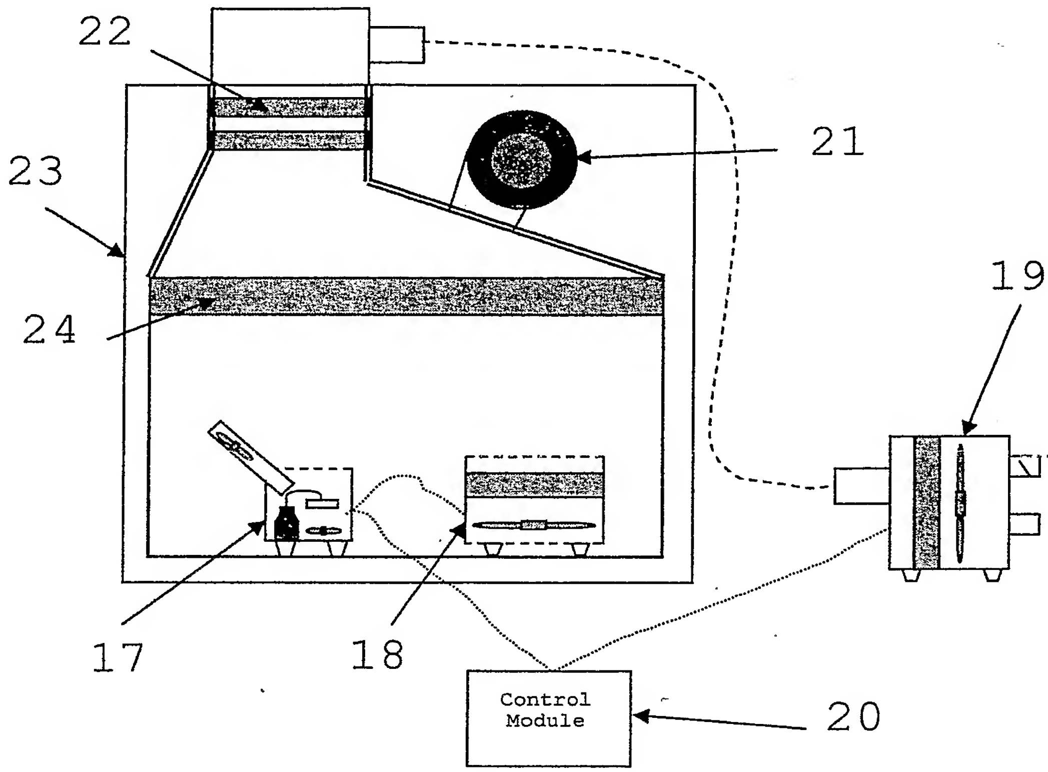

Fig 5

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